Please replace the paragraph at page 7, line 29 to page 8, line 2 with the following amended paragraph:

Figures 5A-B illustrate a nucleotide sequence of the plasmid construct pACSE3 (SEQ. ID. No. 3). Plasmid pACSE3 differs from plasmid pACSE2 of Figures 3 and 4A-B only by modification of several restriction sites. Specifically, base 534 was changed from C to T and base 539 was changed from G to A in order to convert the unique NcoI site to a BspHI site, while base 653 was changed from A to T to destroy the existing BspHI site and base 3218 was changed from A to T to destroy existing BspHI site. The unique BspHI site, which extends from bases 534-539, is underlined.

In the Claims:

Please cancel claims 11 and 14 without prejudice and replace claims 1, 4, 12, 13, 15, 18, 22, 24, 25, 30, and 32 as amended below.

1. (Amended) A method of predicting the evolutionary potential of a mutant resistance gene comprising:

preparing a mutant resistance gene that confers a selectable resistance phenotype to a host cell, said preparing comprising successive rounds of mutagenesis and selection until no further enhancement of the resistance phenotype is perceived, the mutant resistance gene either including two or more nucleic acid modifications or encoding a mutant polypeptide including two or more amino acid modifications; and

determining whether the mutant resistance gene is likely to evolve through two or more independent mutation events, where each independent mutation event confers an enhancement of the resistance phenotype.

4. (Amended) The method according to claim 2, wherein said determining comprises:

identifying two or more mutations of the mutant resistance gene which affect the amino acid sequence of the mutant polypeptide;

preparing a first set of singly mutated resistance genes each of which encodes a singly mutated polypeptide consisting of one of the two or more amino acid modifications of the mutant polypeptide;

inserting each of the first set of singly mutated resistance genes individually into one of a first set of host cells; and

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selecting one or more of the first set of singly mutated resistance genes which confer a selectable enhancement of the resistance phenotype to the host cells of the first set, wherein the absence of any selected singly mutated resistance genes indicates that the mutant resistance gene is unlikely to evolve through independent mutations.

12. (Amended) The method according to claim 4, further comprising:

modifying the selected singly mutated resistance genes, wherein said modifying comprises introducing an additional mutation in the selected singly mutated resistance gene to prepare one or more doubly mutated resistance genes each of which encodes a doubly mutated polypeptide;

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inserting each of the one or more doubly mutated resistance genes individually into a second set of host cells; and

selecting one or more of the doubly mutated resistance genes which confers a selectable enhancement of the resistance phenotype to the host cells of the second set.

13. (Amended) The method according claim 12, wherein said selecting one or more of the doubly mutated resistance genes comprises:

introducing the host cells of the second set onto a selection media and

collecting the host cells of the second set which grow on the selection media.

15. (Amended) The method according to claim 14, further comprising:

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repeating the steps of modifying, inserting, selecting, and assessing in succession until each of the two or more mutations of the mutant resistance gene have been recreated, indicating that the mutant resistance gene is likely to evolve through independent mutations.

18. (Amended) The method according to claim 1, wherein said preparing comprises:

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providing a resistance gene;

introducing a plurality of mutations into the resistance gene to produce a mutated resistance gene;

inserting the mutated resistance gene into a host cell;

selecting the host cell which exhibits the strongest resistance phenotype;

isolating the mutated resistance gene from the selected host cell; and

repeating at least one subsequent round of said providing, introducing, inserting, selecting, and isolating until the mutated resistance gene of a subsequent round exhibits no further enhancement of the resistance phenotype relative to the mutated resistance gene of a preceding round.

22. (Amended) The method according to claim 20, wherein the plasmid is selected from the group consisting of pACSE, pACSE2, and pACSE3.

24. (Amended) A method of screening a drug for anti-pathogenic activity against a pathogen including a mutant anti-pathogenic resistance gene, the method comprising:

providing a host cell comprising a mutant anti-pathogenic resistance gene either including two or more nucleic acid modifications or encoding a mutant anti-pathogenic polypeptide which includes two or more amino acid modifications, wherein the mutant anti-pathogenic resistance gene or mutant anti-pathogenic polypeptide confers a selectable advantage to the host cell, the mutant anti-pathogenic resistance gene having been prepared by successive rounds of mutagenesis and selection until no further enhancement of the resistance phenotype is perceived and having been demonstrated to be likely to evolve through two or more independent mutation events, where each independent mutation event confers an enhancement of the resistance phenotype;

growing the host cell on a selection media comprising a candidate drug or combinations thereof; and

determining whether the host cell is capable of growing on the selection media, wherein absence of host cell growth and/or proliferation indicates anti-pathogenic activity for the candidate drug or combinations thereof.

25. (Amended) The method according to claim 24, wherein said providing the host cell comprises:

providing an anti-pathogenic resistance gene;

introducing a plurality of mutations into the anti-pathogenic resistance gene to produce a mutated anti-pathogenic resistance gene;

inserting the mutated anti-pathogenic resistance gene into a host cell;

selecting the host cell which exhibits the strongest resistance phenotype;

isolating the mutated resistance gene from the selected host cell;

repeating said providing, introducing, inserting, selecting, and isolating until the mutated resistance gene of a subsequent round exhibits no further enhancement of the resistance phenotype relative to the mutated resistance gene of a preceding round; and

determining whether the mutant resistance gene is likely to evolve through two or more independent mutation events, where each independent mutation event confers an enhancement of the resistance phenotype.

30. (Amended) The method according to claim 25, wherein said inserting is carried out by

ligating the mutated anti-pathogenic resistance gene into a plasmid and

treating the host cell under conditions effective to incorporate the plasmid into the host cell.

32. (Amended) The method according to claim 30, wherein the plasmid is selected from the group consisting of pACSE, pACSE2, and pACSE3.